

may be used in methods for identifying compounds useful for the treatment of a disease, *e.g.*, AIDS and HIV-related disorders. In addition, a differentially expressed gene involved in a disease may represent a target gene such that modulation of the level of target gene expression or of target gene product activity will act to cure, heal, alleviate, relieve, alter, remedy, ameliorate, improve or affect a disease condition, *e.g.*, AIDS and HIV-related disorders. Compounds that modulate target gene expression or activity of the target gene product can be used in the treatment of a disease. Although the genes described herein may be differentially expressed with respect to a disease, and/or their products may interact with gene products important to a disease, the genes may also be involved in mechanisms important to additional disease cell processes.

[0012] An "AIDS- or HIV-related cell", as used herein, includes, but is not limited to, thymocytes, dendritic cells, T cells, macrophages, peripheral blood mononuclear cells (PBMC), lymphocytes, monocytes, leukocytes and lymphoid cells.

Molecules of the Present Invention

Gene ID 9145

[0013] The human 9145 sequence, known also as 11 β -hydroxysteroid dehydrogenase (11 β -HSD), is approximately 1348 nucleotides long including untranslated regions (SEQ ID NO:1). The coding sequence, located at about nucleic acid 102 to 980 of SEQ ID NO:1, encodes a 292 amino acid protein (SEQ ID NO:2).

[0014] As assessed by TaqMan analysis, 9145 mRNA expression was detected in thymocytes, dendritic cells, dendritic cell CD4+ T cell (DC/CD4) cocultures, T cells and macrophages. 9145 mRNA expression was highly induced by HIV infection in dendritic cells, DC/CD4, macrophages and thymocytes, and CD4+ T cells.

[0015] 9145 catalyzes the conversion of inactive cortisone to the active glucocorticoid cortisol. The principal glucocorticoid is cortisol. Cortisol is known to have a number of immunosuppressive effects including inhibition of mediators of inflammation, such as cytokines and prostaglandins. Cortisol inhibits production of IL-1 and IL-6 from macrophages and the production of inflammatory effects of bradykinin, platelet-activating factor and serotonin. Cortisol levels are elevated in HIV infected individuals which are correlated with disease progression. HIV patients have been demonstrated to have increased

sensitivity to glucocorticoids due to enhanced receptor expression (*The Journal of Immunology*, 2002, 169: 6361-6368). 9145 mRNA expression is primarily restricted to T cells, dendritic cells, macrophages and liver which contain large numbers of monocyte derived Kupfer cells. 9145 is induced to very high levels of expression following T cell and macrophage activation and following infection with HIV. The induction of 9145 may lead to increased cortisol levels locally and perhaps systemically which could lead to reduced immune responses including the production of proinflammatory cytokines, cytotoxic T cell and NK cell killing of virus-infected cells and enhanced viral replication. Therefore, inhibition of 9145 may decrease glucocorticoid levels, inhibit HIV replication and prevent the immunosuppressive effects of cortisol.

[0016] Due to 9145 mRNA expression in thymocytes, dendritic cells, dendritic cell CD4+ T cell (DC/CD4) cocultures, T cells and macrophages, along with its functional role, modulators of 9145 activity would be useful in treating AIDS and HIV-related disorders. 9145 polypeptides of the present invention are useful to screen for modulators of 9145 activity.

Gene ID 1725

[0017] The human 1725 sequence (SEQ ID NO:3), known also as angiotensin-converting enzyme, testis-specific isoform (ACE-T), is approximately 2478 nucleotides long including untranslated regions. The coding sequence, located at about nucleic acid 29 to 2227 of SEQ ID NO:3, encodes a 732 amino acid protein (SEQ ID NO:4).

[0018] As assessed by TaqMan analysis, 1725 mRNA was highly expressed in macrophages, PBMC, tonsil and lymph node. 1725 mRNA was induced by HIV infection of CD4+ T cells, thymocytes, dendritic cells, dendritic cell/CD4+ T co-cultures and was highly expressed in the permissive Jurkat T cell clone 10H.

[0019] 1725 is a protease that is expressed at high levels in lymphocytes, dendritic cells and macrophages. 1725 is induced in macrophages by CD4+T cells (*Clin Exp Immunol*, 1992, 88(2):288-94) and is known to be involved in activation of CD4+ T cells. 1725 also has high levels of expression in lymphocytes, dendritic cells and macrophages when induced by HIV infection. 1725 is involved in T cell activation required for HIV replication. Therefore, antagonizing 1725 would inhibit HIV replication.

[0020] Due to 1725 mRNA expression in macrophages, PBMC, tonsil and lymph node, along with its functional role, modulators of 1725 activity would be useful in treating

AIDS and HIV-related disorders. 1725 polypeptides of the present invention are useful to screen for modulators of 1725 activity.

Gene ID 311

[0021] The human 311 sequence (SEQ ID NO:5), known also as the nicotinic acid receptor (HM74A), is approximately 2051 nucleotides long including untranslated regions. The coding sequence, located at about nucleic acid 61 to 1224 of SEQ ID NO:5, encodes a 387 amino acid protein (SEQ ID NO:6).

[0022] As assessed by TaqMan analysis, 311 mRNA was highly expressed in spleen, tonsil, lymph node and PBMC. 311 mRNA was induced by HIV infection of dendritic cells, dendritic cell/T cell co-cultures and macrophages.

[0023] 311 is the nicotinic acid receptor, HM74A (*JBC*, 2003, 278:9869-9874). Administration of nicotinic acid is used in the treatment of dyslipidemia which is believed to inhibit adipocyte lipolysis via the activation of a Gi-coupled receptor. Gi-coupled receptor stimulation results in the activation of MAP and JNK kinases which are involved in the production of cytokines and cell division. HIV replication requires T cell activation. Antagonizing 311 would result in decreased T cell activation and viral replication.

[0024] Due to 311 mRNA expression in the spleen, tonsil, lymph node and PBMC, along with its functional role, modulators of 311 activity would be useful in treating AIDS and HIV-related disorders. 311 polypeptides of the present invention are useful to screen for modulators of 311 activity.

Gene ID 837

[0025] The human 837 sequence (SEQ ID NO:7), known also as the alpha 7 subunit of the acetylcholine receptor, is approximately 2087 nucleotides long including untranslated regions. The coding sequence, located at about nucleic acid 104 to 1612 of SEQ ID NO:7, encodes a 502 amino acid protein (SEQ ID NO:8).

[0026] As assessed by TaqMan analysis, 837 mRNA was highly expressed in peripheral blood lymphocytes (PBL) and tonsil. 837 mRNA was induced by HIV infection of CD4+ T cells, thymocytes, dendritic cells, dendritic cell/CD4+ T co-cultures.

[0027] 837 is required for an anti-inflammatory response that inhibits TNF α secretion by macrophages (*Nature*, May 2000, 405(6785):458-462). 837 knockouts display elevated levels of TNF α . TNF α is secreted by macrophages, which enhances HIV